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Can Clinical Reminder Help Optimize the Use of Secondary Prevention Therapies in Non-ST Elevation Acute Coronary Syndrome?

Anatoly Langer[1,2],
Mary Tan[1],
Tomas Cieza[3],
Robert Ciomyk,
John Graham[2],
Krishnan Ramanathan,
René Hamel[4],
Virginie Bernier[4],
Shaun G Goodman[1,2]

[1]Canadian Heart Research Centre, Toronto, Ontario, Canada
[2]St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada
[3]Quebec Heart and Lungs Institute and University Laval, Quebec, Canada
[4]Servier Canada Inc, Laval, Quebec, Canada

Abstract

Patients with ACS remain at high risk of major coronary events and require further therapy to improve their survival and lower morbidity.

A total of 35 Canadian hospitals participated and enrolled NSTEMI ACS patients admitted with the first event. Patients surviving to hospital discharge were followed up at 4 and 6 months to assess the use of recommended secondary prevention measures. Physicians were reminded of the recommended secondary prevention measures by way of a clinical reminder which was shown if an individual patient management did not conform to the recommendations.

A total of 423 patients (70% male) who were 63.4 ± 11.2 years old were recruited by 28 hospitals. Systolic and diastolic BP was 140 ± 23 and 80 ± 14 mmHg, respectively and the heart rate was 75±15 beats per minute. Time from symptom onset to presentation was 1-12 hours in 57%, 12-24 hours in 20%, and > 24 hours in 23%. Presenting ECG was normal in 43%, revealed T wave inversion in 30%, ST segment depression in 26% and non-specific changes in 18%. While in hospital 93% of patients had an angiogram, PCI was performed in 67% and CABG in 12%. Recommended secondary prevention measures were prescribed in only 31% of patients at hospital discharge; the use of the clinical reminder was associated with significant increase in secondary prevention treatments during the follow up (p =0.0072).

Simple clinical reminders offered as part of the electronic data entry appear feasible and may support optimizing patient care based on guidelines and recommendations.

Introduction

Development of an Acute Coronary Syndrome (ACS) represents a significant event in the natural history of a patient with Coronary Artery Disease (CAD). The likelihood of mortality and significant morbidity is greatly elevated at this time and remains so at least for the next 12-24 months. Effective management of patients at this point in the pathophysiologic cascade of their disease provides an important and unique opportunity to save and improve lives [1-3] and the importance of optimal (evidence-based) dosing post ACS and the need for up titration of beta-blockers, statins, and Angiotensin-Converting Enzyme Inhibitors (ACEI)/Angiotensin II Receptor Blockers (ARBs) at discharge and 12 months post ACS discharge has been identified as one of the key performance measures [4].

Despite available data and treatment recommendations for patients with non-ST elevation (NSTE) ACS [5,6] recent registry data suggest that patients with ACS frequently do not receive recommended treatment and that this care gap leads to less than optimal outcome [7-13]. We recently examined in detail the reasons for suboptimal use of evidence-based therapies at hospital discharge and after 1 year from the perspective of both the physician and the patient in a large cohort of unselected NSTE ACS patients [8]. The main findings were that in patients without specific contraindications or proven drug intolerance, the most common reason for not prescribing antiplatelet, statin or Angiotensin Converting Enzyme Inhibitor (ACEI) was the physician's subjective assessment that the patient was "not high-enough risk" or that there was "no evidence/guideline to support use". Furthermore, after 1 year, 77% of patients not on optimal medical therapy at discharge remained without optimal treatment, and overall use of evidence-based therapies declined. These findings based on prior experience in ACS I and II programs conducted by the Canadian Heart Research Centre (CHRC) [7-13] formed the basis of the current program aimed at improving the use of optimal therapy at hospital discharge and beyond using a clinical reminder to alert physicians when management differed from evidence based publications or recommendations. The primary objective and end point of this Medical Practice Activity

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*Corresponding author:

Langer A
Canadian Heart Research Centre
Toronto, Ontario, Canada
Tel: 416.977.8010, ext 253
Mobile: 416.999.6264
Fax: 1.866.562-976
E-mail: langera@CHRC.net

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(MPA) was proportion of patients achieving the use of recommended therapy during the follow up. We have previously documented that the use of clinical reminders may be helpful in achieving recommended targets [14], though the success in adherence to the guidelines can be variable [15]. We defined the use of recommended therapy narrowly based on our prior publication (6) with focus on the use of clinical reminder rather than the therapy itself.

Methods

ACS III was developed by the CHRC as an evidence-based, medical practice activity. The authors developed patient chart audit forms, educational tools, and assisted with the provision of relevant resources for use by participating physicians. The key feature of the data collection was an interactive application, the clinical reminder, whereby physicians were reminded of the recommended therapies at the time of their data entry and in cases when recommended treatment was not used. The program was supported by Servier Canada which funded CHRC at arm's length to engage 40 Canadian hospitals and to enroll 800 patients. Invitations were sent to cardiologists at identified institutions across Canada by e-mail and facsimiles by the CHRC including those who were participants in prior or ongoing registries with the CHRC. Primary care physicians were only approached after patient enrolment and asked to complete follow up. Physicians were reimbursed for their time involvement. The program was reviewed and approved by Institutional Ethics Boards and OPTIMUM Clinical Research, an independent central ethics review board. All aspects of the program deployment, including data capture using eCRF were coordinated by the CHRC and the ownership of all data resided with the CHRC. Patient enrolment started in September 2014 and ended in April 2016 with data entry for follow up completed in March 2017. Inclusion criteria were adults ≥ 18 years old hospitalized and who survived to discharge home from the enrolling institution with a first episode of NSTEMI defined as patients presenting with symptoms suspicious of myocardial ischemia in association with diagnostic elevation in Troponin (Tn) and in whom patient follow up was deemed possible by their primary care physician or specialist whose contact information was known at the time of enrolment. The exclusion criteria were prior ACS event, hemodynamic instability requiring further intervention or support, procedure planned in the next six months such as Coronary Artery Bypass Graft (CABG) surgery, Percutaneous Coronary Intervention (PCI) or pacemaker, significant cardiovascular complications such as LV dysfunction or atrial fibrillation, patient not available or not suitable for follow-up, known sensitivity to recommended therapy, significant renal (eGFR < 15 ml/min) or liver disease, verbal confirmation of pregnancy, or use of investigational drug or device during the program. Patients were seen on three occasions (hospital discharge and two more clinically driven visits at 4 ± 1 month and 6 ± 1 month.

The eCRF developed and deployed by CHRC allowed gathering of clinically relevant variables and had an interactive clinical reminder step during which physicians were reminded of recommended therapy consisting of dual antiplatelet therapy (DAPT: ASA 81 mg daily and ticagrelor 90 mg twice daily), statin therapy (atorvastatin 80 mg daily) and ACEI (ramipril 10 mg or perindopril 8 mg daily).

The co-primary outcome of the MPA was proportion of patients receiving recommended therapy at discharge and last follow up. Descriptive analyses of demographic variables were performed. Continuous variables were summarized as a mean and standard deviation or as a median and discrete variables were reported as counts and percentages. Changes in treatment during follow up were compared using Pearson chi-square test. All analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC, USA).

Results

A total of 423 patients (70% male) who were 63.4 ± 11.2 years old were recruited by 28 hospitals (35 hospitals were activated to enroll but 7 did not enroll any patients): 11 hopsitals in Ontario, 8 in Quebec, 4 in New Brunswick, 2 in Alberta and one each in BC and Saskatchewan.

On hospital admission 91% were Caucasian, 3% south-east Asian, 2% south-Asian, 2% Aboriginal Canadian, 1% each Hispanic and Black and 1% other. Systolic and diastolic BP was 140 ± 23 and 80 ± 14 mmHg, respectively and the heart rate was 75 ± 15 beats per minute. The Killip class was I in 93%, II in 5%, III in 1.8%, and IV in 0.2%; the BMI was 28.8 ± 5.5 kg/m^2. Time from symptom onset to presentation was 1-12 hours in 57%, 12-24 hours in 20%, and > 24 hours in 23%. Presenting ECG was normal in 43%, revealed T wave inversion only in 30%, ST segment depression only in 26% and non-specific changes in 18% and remainder a combination of the above. Medical history was prior cardiovascular disease in 5%, diabetes mellitus in 24%, hypertension in 61%, dyslipidemia in 55%, chronic kidney disease in 8%, smoking history in 64%, chronic obstructive pulmonary disease in 10%. While in hospital 93% of patients had an angiogram showing single, double, triple, left main (LM) and no disease in 44%, 26%, 21%, 3%, and 6% respectively. PCI was performed in 67% involving LAD, RCA, Cx, and LM in 53%, 40%, 34%, and 3% respectively. CABG was performed in 12% involving LAD, RCA, Cx, and LM in 98%, 72%, 84%, and 22% respectively. Assessment of the LV function was undertaken in 72%, mostly by echocardiography (91%) and was normal in 81% and mildly moderately, or severely abnormal in 17%, 2% and 0.3%.

Characteristics	Proportion of patients (N=423)
Prior cardiovascular disease	5%
Diabetes mellitus	24%
Hypertension	61%
Chronic kidney disease	8%
Dyslipidemia	55%
Chronic obstructive pulmonary disease	10%
History of Smoking	64%

Table 1: Medical history

In hospital medical treatment included ASA in 99%, clopidogrel in 47%, ticagrelor in 62%, prasugrel in 0.7%, glycoprotein IIb/IIIa inhibitor in 1.0%, unfractionated heparin in 32%, low molecular weight heparin in 55%, bivalirudin in 1%, diuretic in 14%, ACEI in 73%, angiotensin receptor blocker (ARB) in 8%, statin in 94%, intravenous nitroglycerine in 15%, inotrope in 1%, beta blocker in 78%, and anti-arrhythmic in 1%.

The median (25th, 75th percentiles) length of hospital stay was 4 (3,7) days and on discharge 92% were in Canadian Cardiovascular Society class I, 7% in II, and <1% in III or IV.

During follow up 0.5% died, 0.75% were hospitalized, 1.4% of patients withdrew consent, 27% were no show or lost to follow up for both follow up visits.

The impact of clinical reminders on risk factor control

There were no changes in blood pressure or heart rate during the follow up. Lifestyle modification was recommended in 98% of patients across all three observational periods.

Overall changes in the use of recommended secondary prevention are shown in Figure 1 and demonstrated an improvement over time although there was no immediate change in the prescription of the recommended therapy after the clinical reminder was shown. Those patients not on optimal therapy at baseline had significant increase in the use of optimal therapy during follow up at visit 2 (9.8%) and 3 (15%, p <0.0001).

More detailed analysis revealed that ASA was used 98% of the time across all visits; however, ticagrelor was used in only 59% of patients at baseline and 62% during follow up (p = 0.49). Clopidogrel was used in 47% at baseline, 34.2% and 33% at visits 2 and 3 respectively. The reasons for not using ticagrelor at discharge were believe appropriate management/disagreement with recommendations in 45%, coverage/reimbursement difficulties in 20%, use of other second antipletelet agent in 18% (17% clopidogrel and 1% prasugrel), medical (14%) or social (3%) constraint, or age of the patient in 1%.

The overall use of atorvastatin did not change across observations (75%), however, the use of the recommended 80 mg dose did; from 32% at discharge to 44% at visit 3. (p = 0.015). Similarly, the 40 mg dose of atorvastatin also increased in use from 12% at discharge to 22% at visit 3 (p = 0.001). Interestingly, non atorvastatin use of statin therapy also increased from 14% at discharge to 22% at visit 3. This intensification of lipi d lowering therapy resulted in the lowering of the LDL-C (Table 1) and an increase in the proportion of patients achieving the recommended target of LDL-C < 2.0 mmol/L from 28% to 75%. (p < 0.0001). The reason recommended dose of atrovastatin was not used were believe appropriate management/disagreement with recommendations in 74%, myalgia in 10%, medical constraint in 7%, intolerance for other than myalgia reasons in 3%, age of the patient in 5% and patient refusal in 1%. A total of 28 patients (6.6%) were not on any statin through the study period.

The use of recommended ACEI (ramipril or perindopril) was 62% at discharge and increased to 70% at visit 3 (p = 0.031) and the use of other ACEI was minimal: 1% at discharge and 2% at visit 3 while ARB was prescribed in 8% at discharge and 12% in visit 3. The reason for not prescribing recommended ACEI were believe appropriate management/disagreement with recommendations in 34%, intolerance in 37% (low BP in 25%, cough in 6%, other 6%), medical (27%) or social (1%) constraints or age of the patient in 1%.

The proportion of patients and the reasons for not following the recommendations did not differ between primary care physicians or specialists performing the follow up.

Discussion

The results of ACS III MPA demonstrate that while many of the high risk patients post ACS are not treated according to the published guidelines, further optimization of therapy might be achieved with a clinical reminder which could result in a significant almost a third improvement in adherence to the recommendations (Figure 1).

We have previously demonstrated consistent care gap in ACS patients [7-13] which we defined as a proportion of patients that are not treated according to peer-reviewed recommendations. We have also previously calculated the impact of guidelines adherence among the high risk Canadians [16].

Our findings indicate that class of therapy identified in the recommendations is used more frequently than the specific medication at a specific dose even though the importance of optimal (evidence-based) dosing of specific agents post ACS and the need for up titration post-discharge to achieve optimal doses has been identified as a key performance measure [4]. This treatment inertia is not clearly understood and has been noted and discussed previously [17]. We believe it may have origins in the fear of higher doses being related to higher incidence of side effects or lack of familiarity with specific dosing used in the clinical trial [4]. Thus, physicians may use statin or ACE inhibitor doses familiar to them for management of dyslipidemia or hypertension respectively rather than the use of evidence-based doses for prevention of cardiovascular morbidity and mortality (knowledge gap). Our results over a short period of time suggest that this treatment inertia and knowledge gap may be overcome to some degree with the use of clinical reminder.

Our findings indicate that clinical reminder is an easily deployed tool that may provide support for optimizing patient care in a short period of time. We also found that clinicians were responsive to nuances of recommendations as exemplified by greater use of specific medications and dose recommendations as well as treatment classes when targets for specific treatment were provided.

In-Hospital procedures	Baseline N =423, Proportion of patients
Angiogram	93%
Among those with angiogram done (n=393) One vessel disease Two vessel disease Three vessel disease Left main Normal	 44% 26% 21% 3% 6%
PCI	67%
Among those with PCI done (n=283) LAD Cx RCA LM	 53% 34% 40% 3%
CABG	50 (11.8)
Among those with CABG done (n=50) LAD Cx RCA LM	 98% 84% 72% 22%
Arrhythmia/EP procedures	0.5%
Graded exercise test	4%
Among those with GXT done (n=18) Abnormal Normal	 50% 50%
LV Assessment	72%
Among those with LV assessment (n=306), EF% > 50% (normal) 35-50% (mild) 20-34% (moderate) <20% (severe)	 81% 17% 2% 0.3%

Table 2: In-Hospital Procedures

	V1 (Baseline) N=423	Visit 2 (4 months) N=298	Visit 3 (6 months) N=242
Serum creatinine (µmol/L)	88 ± 57	85 ± 29	81 ± 24
eGFR	87.5 ± 47.5*	77.4 ± 20.4	75.9 ± 21.2
A1c (%)	6.5 ± 1	6.4 ± 1.1	6.4 ± 1.1
Fasting plasma glucose (mmol/L)	6.4 ± 2.1	6.2 ± 1.5	6.2 ± 1.7
Total cholesterol (mmol/L)	4.6 ± 1.3	3.2 ± 0.9	3.5 ± 1.0
HDL (mmol/L)	1.1 ± 0.5	1.1 ± 0.3	1.1 ± 0.3
LDL (mmol/L)	2.7 ± 1.1	1.6 ± 0.6	1.7 ± 0.6
Triglyceride (mmol/L)	1.9 ± 1.0	1.5 ± 0.7	1.4 ± 0.7

Table 3: Laboratory measures during the follow up
*Calculated using Modification of Diet in Renal Disease (MDRD) formula as lab value was not collected

Limitations

The design of our data set acquisition could not exclude the bias of physician selection, patient selection, or the Hawthorne effect

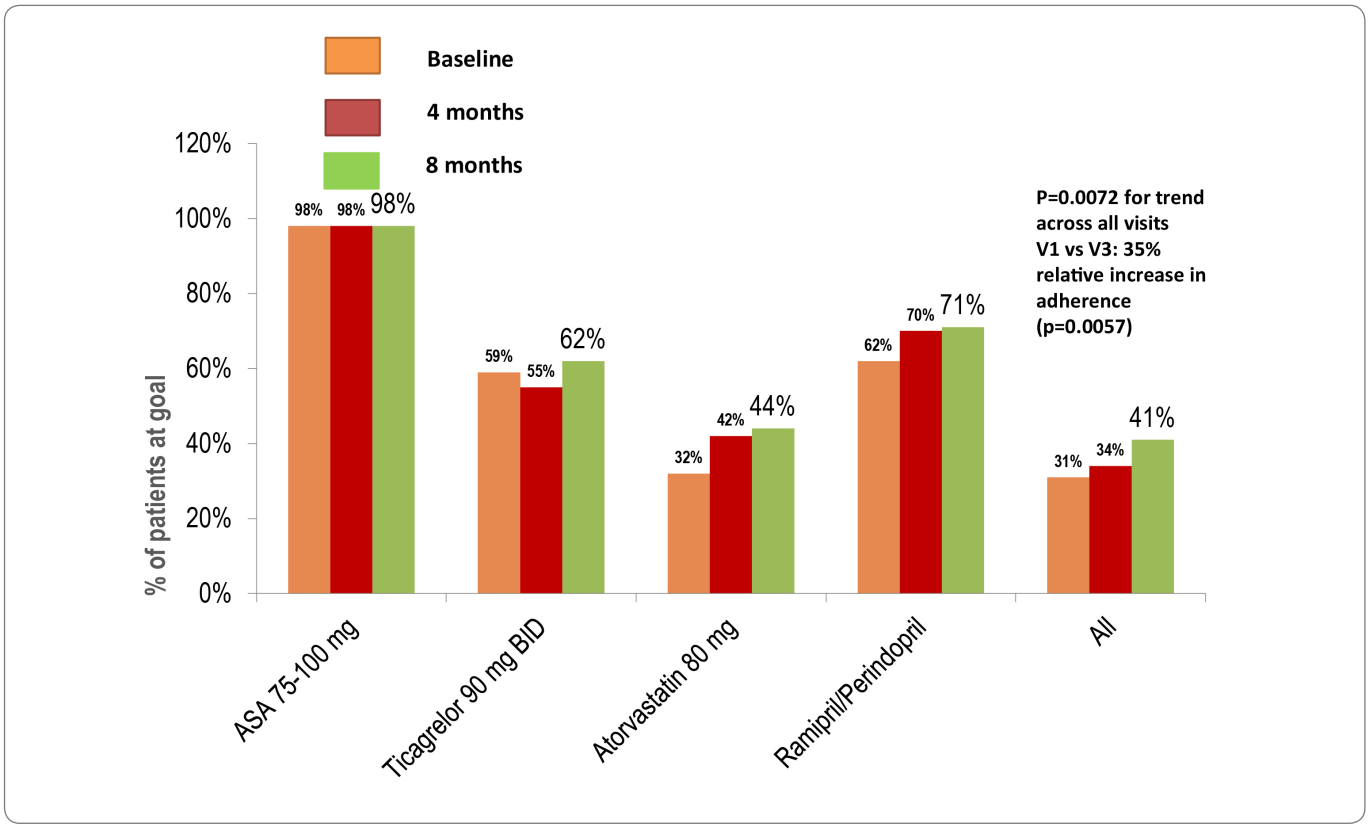

Figure 1: Proportion of patients achieving guidelines recommended treatment.

(the modification of behavior of the participating physicians due to their awareness of being monitored). We did not measure the use of other recommended interventions such as smoking cessation, though lifestyle modification recommendation was recorded as being provided in almost all patients. Relatively high dropout rate, while reflective of the clinically driven follow up, likely contributed to an already relatively small sample size resulting in less reliable ascertainment of the care gap and the ability to assess the impact of the clinical reminder. Lack of the control group makes our findings of the clinical reminder benefit less certain. This consideration notwithstanding the overall improvement in adherence to recommended secondary prevention therapies over a period of follow supports our overall conclusion. We used a narrow definition of recommended therapy (e.g. only atorvastatin 80 mg rather than also atorvastatin 40 mg) based on published clinical trials (6) in order to focus specifically on the use of clinical reminder.

Conclusion

The present study highlights the opportunity to overcome treatment inertia. Simple clinical reminders offered as part of the electronic data entry appear to be feasible and may provide support for optimizing patient care post ACS based on guidelines and recommendations.

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